U.S. Serial No.: 10/667,151
Group Art Unit 1611
Examiner Charlesworth Rae

Rejection under 35 U.S.C. 103(a)

Claims 1-13, 19-21, and 38-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gentz et al. (US Patent 6,869,927 B1, "Gentz"). Claims 14-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gentz in view of Flacke et al. (*Circulation*, 2001), and in view of Glajch et al. (US Patent 5,147,631, "Glajch").

In response, Applicants respectfully traverse the rejections and their supporting remarks. Applicants state that the Examiner has not met his burden of establishing a *prima facie* case of obviousness. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest ***all*** the claimed features, either explicitly or inherently. In addition, the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in Applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Applicants state that Gentz et al. fails to teach ***all*** of the claimed elements of the present invention, either explicitly or inherently. The invention of claim 1 is directed to an injectable formulation comprising: (a) a ***chemical ablation agent in an amount effective to cause tissue necrosis***, and (b) a biodisintegrable viscosity adjusting agent in an amount effective to render the formulation highly viscous, wherein said injectable formulation is a sterile injectable formulation.

Gentz et al. does not teach a chemical ablation agent in an amount effective to cause tissue necrosis, as claimed. Indeed, the words "ablation," "necrosis" or "cell death" do not appear anywhere in Gentz et al. There is simply no disclosure of chemical ablation agents or any agents that cause tissue necrosis. Without such explicit teaching, the Examiner appears to be asserting that Gentz et al. teaches this element inherently. According to the Examiner's argument,

Gentz et al. teaches sodium chloride and thus, the sodium chloride inherently reads upon the claimed "chemical ablation agent in an amount effective to cause tissue necrosis."

Applicants respectfully disagree and state that inherency has not been shown. A holding of inherency must flow as a necessary conclusion from the prior art, not simply a possible one. The fact that a certain result or characteristic ***may*** occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 U.S.P.Q.2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); *In re Oelrich*, 666 F.2d 578, 581-82, 212 U.S.P.Q. 323, 326 (CCPA 1981). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.'" *In re Robertson*, 169 F.3d 743, 745, 49 U.S.P.Q.2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted); MPEP 2112 IV.

Thus, the fact that the Examiner believes that the sodium chloride of Gentz et al. ***may*** result in the claimed "chemical ablation agent in an amount effective to cause tissue necrosis" is insufficient to establish inherency. This is doubly true since the sodium chloride-containing formulations of Gentz et al. are expressly ***not*** for promoting cell necrosis and tissue ablation. To the contrary, Gentz et al. teaches adding NaCl to formulations that promote ***tissue growth*** not tissue necrosis. For instance, Gentz et al. discloses "formulations...***to promote or accelerate soft tissue growth or regeneration, for example in wound healing***" (col. 2, lines 14-16)(emphasis added) and such formulations can include "***NaCl***, glycine, sucrose or mannitol, or combinations thereof, as a tonicifier at a concentration of from about 0mM to about 150 mM." (col. 4, lines 33-36)(emphasis added).

The Examiner's assumption that the formulations of Gentz et al. inherently teach chemical ablation is contrary to the basic teaching of Gentz et al., which discloses formulations for "***soft-tissue growth and regeneration***" (col. 2, lines 2-3)(emphasis added). Rather than

reading upon the claimed chemical ablation agent, the disclosure of Gentz et al. would ***teach away*** one of skill in the art from taking the tissue growth supporting NaCl formulation of Gentz et al. to produce the tissue necrotizing formulation of the claimed invention. The Examiner has simply not shown otherwise.

Instead of offering evidence, the Examiner states that "sodium chloride of about 150 mM is reasonably construed to serve as a chemical ablation agent in [an] amount effective to cause tissue necrosis and to reasonably serve as a biodisintegrable viscosity adjusting agent in an amount effective to render the formulation highly viscous." Even if it were assumed that sodium chloride of about 150 mM is of sufficient concentration to cause tissue necrosis, Applicants respectfully state that the formulations of Gentz et al. would appear to not be 150 mM NaCl, as alleged by the Examiner, but rather, are "isotonic" (col. 7, line 61). For example, although several of the examples disclose using "125 nM NaCl," as one of the ingredients in the formulations, it is clear upon close inspection that the NaCl is then diluted with other components. For instance, Gentz et al. discloses that "the lyophilized KGF-2 polypeptide formulations are reconstituted in sterile water so as to maintain ***isotonic*** conditions of about 290 mOsm." (col. 7, lines 47-61)(emphasis added). Another example teaches taking 125 nM NaCl, and mixing it with other components, including "water as diluent." (col. 6, line 19).

As would be appreciated by one of ordinary skill in the art, an ***isotonic*** NaCl solution would ***not*** cause tissue necrosis since one of skill would appreciate that an isotonic solution would have the salinity of normal bodily fluids. Thus, Gentz et al. fails to teach or suggest the claimed ***chemical ablation agent in an amount effective to cause tissue necrosis***. Thus, Applicants submit that inherency has not been shown and respectfully requests that the Examiner reconsider and withdraw the rejection under 35 U.S.C. 102(b).

In addition, given that Gentz et al. is directed to formulations for soft-tissue healing, Applicants state that one of ordinary skill in the art would have no motivation to modify the formulations of Gentz et al. to arrive at the claimed invention. Rather, one of ordinary skill would be dissuaded from using such formulations to necrotize soft-tissue given the teachings of

Gentz et al. Even if it were assumed that such motivation were to exist, Gentz et al. fails to teach or suggest all of the claimed features.

The secondary references fail to remedy the deficiencies of Gentz et al. Neither Flacke or Glajch teaches a chemical ablation agent in an amount effective to cause tissue necrosis. Flacke